

# Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Awardee Workshop

February 15, 2022

## Virtual

### WELCOME AND OPENING REMARKS

#### Welcome and Overview

*Janine Austin Clayton, M.D., FARVO, Director, Office of Research on Women's Health, and NIH Maternal Mortality Task Force Co-Chair*

Dr. Clayton welcomed the attendees and introduced the meeting by noting that it is well known that the United States is the most dangerous place in the developed world to deliver a baby. America's health disparities and high maternal mortality rates are particularly prevalent among American Indian/Alaska Native and African American women, who are two to four times as likely to die as White women are. Women over the age of 35 and those residing in rural areas are also at higher risk.

Multiple factors play a role in these disparities, including social determinants of health (SDOH), structural factors, bias, and healthcare access. It is imperative to leverage these institutional factors moving forward. Each encounter in a person's life course must be viewed in the context of what came before and what came after. Pregnancy and menopause are two critical opportunities in the life course where interventions can greatly affect subsequent health. Researchers must take an integrative, multisystem approach by looking at the entire breadth of the pregnancy experience, from pre-pregnancy to the pregnancy itself to the postpartum period, and take advantage of this window of opportunity for positive change.

A very concerning issue is that in the United States, homicide was the leading cause of death during pregnancy and the postpartum period between 2018 and 2019. Black women's rates of pregnancy-related intimate partner homicide were three times greater than rates among White and Hispanic women. Intimate partner violence can also have a deleterious effect on *in utero* development and subsequent care of the child.

The IMPROVE initiative was created to address the rising rates of pregnancy-related deaths and maternal morbidity (MM). This workshop highlights some of the fiscal year (FY) 2020 IMPROVE award recipients, who will share their preliminary results and identify gaps in maternal research. The meeting is an opportunity to connect these awardees to each other and to the expertise of all the participating NIH institutes and centers (ICs) and help generate an evidence-based approach to maternal health research that will benefit all populations.

#### Opening Remarks

*Diana Bianchi, M.D., Director, NICHD, and NIH Maternal Mortality Task Force Co-Chair*

Dr. Bianchi said that the beginnings of the IMPROVE initiative could be traced to an early morning meeting that she; then–NIH Director Francis Collins, M.D., Ph.D.; and other NIH directors had with the congressional Black Maternal Health Caucus. The Caucus members urged NIH to do more to coordinate NIH-wide research to address health disparities in maternal health. This conversation led to the formation of the NIH Maternal Mortality Task Force to coordinate NIH-wide efforts in obstetrical research. The task force provided the vision and impetus for IMPROVE, an initiative that encompasses both foundational biology and social and biobehavioral research and that incorporates the input of community partners.

IMPROVE focuses on the major causes of maternal morbidity and mortality, including cardiovascular events, infection, and mental and behavioral health, as well as the major social determinants of maternal health, including structural racism and discrimination. For the FY 2020 research administrative supplements, NIH awarded more than \$7 million (mostly from the Office of the Director [OD]) to support 36 projects exploring various causes of maternal deaths (e.g., heart disease, hypertension, bleeding) and contributing conditions (e.g., diabetes, obesity, factors contributing to delays in maternal care). Dr. Bianchi said that the success of the first round of supplements catalyzed an increase in FY 2021 funding to more than \$13 million (from both the OD and the ICs) to support 22 projects. These projects will focus on the impact of the COVID-19 pandemic on maternal health and the effect of structural racism and discrimination on maternal health outcomes in the context of the COVID-19 pandemic.

Dr. Bianchi noted that because the funding is done via supplements, money could only be awarded to researchers who already had NIH grants. However, the proposed budget for FY 2022 sets aside \$30 million for IMPROVE and, if approved, would provide sustainability and allow for funding mechanisms other than administrative supplemental funding.

Dr. Bianchi thanked the members of the task force and the ICs for bringing their perspectives and expertise to IMPROVE. She said there was great excitement about this workshop and the opportunity to hear about the important research being done as part of the IMPROVE initiative.

## **CARDIOVASCULAR RISKS AND PREECLAMPSIA**

### **Moderator**

*Gina S. Wei, M.D., M.P.H., National Heart, Lung, and Blood Institute (NHLBI), NIH*

### **Presentation: A Comorbidity-Based Screening Tool to Predict Severe Maternal Morbidity at the Time of Delivery**

*Kathryn Johnson Gray, M.D., Ph.D., Harvard Medical School*

Pregnancy-related mortality in the United States has been increasing. About 700 women per year died from pregnancy complications (pre-pandemic figures). COVID-19 caused the deaths of 273 pregnant women. There is a great disparity in who dies, and more than 60% of these deaths are preventable. One important question is how to identify at-risk patients earlier so that measures can be taken to reduce morbidity and mortality.

Dr. Gray said that some of her colleagues had developed a tool called the obstetric comorbidity index (OB-CMI) for predicting severe maternal morbidity (SMM). The tool assigns points to various comorbidities and pregnancy conditions (e.g., congestive heart failure = 5 points,

pulmonary hypertension = 4 points, previous cesarean delivery = 1 point), based on pregnancy outcomes from large databases. The tool was used prospectively in clinical care to predict women at risk for SMM at delivery (e.g., a woman with an OB-CMI of 0 had a 0.41% chance of SMM, while a woman with an OB-CMI at or above 9 had an 18.75% chance of SMM).

Dr. Gray said her study looked at whether the OB-CMI tool could be used antenatally (at presentation to prenatal care) to identify patients at risk for SMM by enhancing the tool to integrate LIFECODES, her institution's longitudinal pregnancy biobank. LIFECODES, which started in 2006, has collected data on over 5,000 pregnancies and contains annotated biological measures and clinical data. This enhanced tool might be used to augment OB-CMI's current predictive capabilities to answer other important questions, such as how other sociodemographic factors relate to OB-CMI and whether genetic and biologic predictors of preeclampsia improve SMM risk predictions.

Dr. Gray said she and her team looked at the prevalence of the OB-CMI comorbidities in the LIFECODES population to see what factors influence the prediction model. About 16% of patients have hypertension or preeclampsia, and 3.5% with preeclampsia with severe features. Over 3% had placental accreta or abruption, and 8.9% had a body mass index (BMI) over 40. In comparing OB-CMI scores for patients with and without SMM at delivery, the investigators found significant correlations between the delivery and the ambulatory population's OB-CMI scores. Moreover, in looking at OB-CMI scores from the ambulatory period to delivery, people who experienced SMM at delivery had significant increase in their OB-CMI scores from the initiation of their prenatal care compared with those who did not experience SMM at delivery. Changes during pregnancy, from the time care is initiated through to delivery, are important components of assessing who is at risk. Dr. Gray noted that the change in OB-CMI was largely driven by the development of preeclampsia, gestational diabetes, and BMI above 40, all of which increased the risk of morbidity and placental disorders.

Dr. Gray's team is just starting to explore how other sociodemographic factors relate to OB-CMI, but in looking at maternal race, ethnicity, insurance type, level of education, and conception type, people with a high OB-CMI (i.e.,  $\geq 5$ ) are not concentrated in any of these groups but are represented across all categories.

Dr. Gray said her team next intends to use LIFECODES data to determine whether genetic and biologic predictors of preeclampsia enhance the risk of SMM, particularly because preeclampsia is one of the biggest drivers of change in OB-CMI. The goal is to identify what other factors might predict who will develop preeclampsia and therefore be at high risk for SMM. This investigation, conducted in conjunction with the Boston-Colombia Collaborative for Adverse Pregnancy Outcomes (BCC-PREG), will involve whole genome sequencing of maternal and fetal samples in LIFECODES and samples from Dr. Gray's Trans-Omics for Precision Medicine (TOPMed) project. The BCC-PREG project will sequence 14,615 multi-ancestral (i.e., European, African, Hispanic/Latino, Asian, and other) maternal and offspring samples. This work will provide genetic and omic data to integrate with measures of comorbidity in LIFECODES to determine other predictors that could improve the prediction of SMM at delivery.

Dr. Gray summarized the answers to the study questions so far:

- *Can OB-CMI be used antenatally to identify patients at risk for SMM?* Yes, and the changes from the antenatal OB-CMI to delivery OB-CMI are important.
- *How do other sociodemographic factors relate to OB-CMI?* Increased OB-CMI is prevalent across sociodemographic categories.
- *Do genetic and biologic predictors of preeclampsia enhance SMM risk prediction beyond the OB-CMI?* Predicting how other factors will integrate with OB-CMI is an important area of ongoing work.

### *Discussion*

*What are the demographics of the LIFECODES patients—specifically, the minority representation? This affects the generalizability of the findings.* **Dr. Gray** said the LIFECODES population is 50% White, 20% Black, 15% Asian, and 15% Hispanic.

*Since maternal morbidity and mortality extends postpartum, are there plans to do analyses on the predictability of the OB-CMI tool in the postpartum period?* **Dr. Gray** said the team intends to look at the postpartum period to identify cases of SMM, and expects to follow cardiovascular events and their relationship to the OB-CMI score for an even longer period.

*What will be learned from the genetic data, and how will that information be used for prediction models?* **Dr. Gray** said more exploration is needed, but it appears that mothers who have a genetic predisposition to hypertension are at much higher risk of preeclampsia. Identifying the specific biologic pathways for people who have that genetic predisposition, and perhaps ultimately integrating that into care, may be a way to understand the risk that is present.

### **Presentation: Severe Maternal Morbidity During Delivery Hospitalization Within an Integrated Healthcare System: Racial and Ethnic Disparities Related to Chronic Hypertension and Preeclampsia**

*Erica Pauline Gunderson, Ph.D., M.S., Kaiser Permanente Bernard J. Tyson School of Medicine, Northern California Division of Research*

SMM affects up to 3% of U.S. pregnancies, and preeclampsia is a leading risk factor for SMM. Black women have a twofold higher rate of preexisting chronic hypertension (cHTN) compared with White women, possibly contributing to the racial and ethnic disparities in maternal health outcomes. Dr. Gunderson said her study was designed to evaluate the role of cHTN and hypertensive disorders of pregnancy (HDP) in relation to SMM and racial and ethnic disparities and to identify the joint association of prior cHTN and preeclampsia with the relative risk of SMM, accounting for clinical, lifestyle, and social factors. The study used Kaiser Permanente electronic health records (EHRs) to look at deliveries involving one singleton pregnancy (live or stillbirth) among women 18 to 45 years old in Northern California from 2009 to 2019. Women with cHTN and diabetes were included, but women with other serious diseases and women with a history of preeclampsia were excluded. There were two cohorts: women with prior cHTN ( $n = 13,626$ ) and a low-risk cohort composed of women with no cHTN and no history of preeclampsia ( $n = 249,892$ ).

The racial and ethnic composition of the total sample (i.e., both cohorts) was 25% Asian, 8%

Black, 26% Hispanic, 37% White, and less than 1% American Indian/Alaskan Native. The low-risk cohort had a racial and ethnic breakdown similar to that of the total sample, but in the prior cHTN cohort, Black women made up 14% and Asian women made up 20%. In terms of age and pre-pregnancy BMI, the Black, Hispanic, and Native Hawaiian/Pacific Islander groups were slightly younger (i.e., < 30 years old) and had a higher percentage of obesity, which is a risk factor for cHTN and preeclampsia. The investigators used the Neighborhood Deprivation Index to assess social determinant risk factors and found that these same three groups were also the most or more deprived.

The investigators estimated the proportion of women with SMM in their sample was 5,589 women, or 2.1% of the total study population. When SMM distribution (i.e., number per 10,000 births) was compared between women with no cHTN and those with prior cHTN, stratified by race and ethnic groups, higher numbers of SMM were associated with prior cHTN across all groups. Higher SMM numbers (per 10,000 births) were observed in the Native Hawaiian/Pacific Islander group (1167), followed by the Asian (711), Black (688), Hispanic (618), and White (488) groups. The investigators also looked at cHTN and HDP outcomes in the racial and ethnic groups, finding that women who developed preeclampsia had similar occurrences of SMM, regardless of whether they had no cHTN or prior cHTN, with the Native Hawaiian/Pacific Islander group at the highest risk for SMM. Preeclampsia in women with prior cHTN was highest in the Native Hawaiian/Pacific Islander group (44.1%), followed by the Asian (36.2%), Hispanic (34.0%), Black (32.0%), White (26.1%), and American Indian/Alaska Native (23.3%) groups. Women with no prior cHTN or history of preeclampsia had much lower percentages of preeclampsia (the highest being 6.1% for Black women, versus 4.4% for White women), and lower percentages of gestational hypertension (the highest being 5.6% for White women, versus 5.2% for Black women).

For the final analysis of the risk factors, Dr. Gunderson presented a model of the adjusted odds ratios of SMM, stratified by cHTN and HDP among the racial and ethnic groups, using the White group as the reference group. Overall, non-white women who developed preeclampsia, whether or not they had prior cHTN, had at least six-fold higher odds of SMM at delivery hospitalization compared with women in the White group who developed preeclampsia. This pattern is also consistently observed when stratified by specific race-ethnic groups.

Dr. Gunderson summarized the study findings:

- Both cHTN and preeclampsia are related to a higher risk of SMM during hospitalization for delivery.
- Preeclampsia showed comparable high rates of SMM for groups with prior cHTN and without cHTN across all race and ethnicity groups.
- Hawaiian/Pacific Islander individuals had the highest rates of SMM, followed by Black, Asian, and Hispanic groups, independent of age, obesity, smoking, and social factors.
- Identification and modification of SMM risk factors are crucial to eliminating maternal health disparities.

## Discussion

*Within the Asian American population, there are different subgroups with different cultures and different metabolic risk factors. Do you have the ability to separate these data and aggregate them by different Asian American subgroups?* **Dr. Gunderson** said the investigators do have the ability and the granular data to determine and validate those different groupings. She noted that the investigators had published separately on Filipinos because of that population's much higher risk of peripartum cardiomyopathy.

*You mentioned controlling for obesity, smoking, and social factors in your regression models. What variables constituted the social factors? Also, what accounts for the significantly higher odds ratios of SMM in the Native Hawaiian/Pacific Islander group?* **Dr. Gunderson** said she did not know why the odds ratios were so high with the Native Hawaiian/Pacific Islander group, which comprised about 2,000 women out of the 240,000 women in the sample. She noted this group has higher rates of severe obesity and may have more cHTN, but more study is needed. The Neighborhood Deprivation Index was used for social factors, and a Kaiser Permanente task force is looking into measuring social factors and obtaining them from EHRs.

## **Presentation: Neurovascular Unit Dysfunction in Women with Severe Preeclampsia**

*Eliza Miller, M.D., M.S., Columbia University*

Dr. Miller said her interest in preeclampsia stemmed from her time training in vascular neurology, when she saw a number of postpartum patients who had had serious strokes or other acute cerebrovascular conditions, many of which caused severe morbidity or death. According to the Centers for Disease Control and Prevention (CDC), cerebrovascular accidents account for 8.2% of pregnancy-related deaths in the United States, with hypertensive disorders of pregnancy (HDP) causing 7.2% of pregnancy-related deaths. Dr. Miller said some studies have shown that the actual mechanism of death in the HDP group was intracerebral hemorrhage, a severe complication of preeclampsia and eclampsia. She described a case study of a 30-year-old African American woman who developed a severe headache about 2 days after delivery and was prescribed pain medication and sent home. The patient presented on postpartum day 8 with generalized seizures and was diagnosed with eclampsia. Radiography of her brain showed posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction in the brain's blood vessels, both well-known effects of the eclampsia syndrome. The woman survived but was permanently disabled. Dr. Miller said she reviewed a number of cases and found a predominance of devastating maternal hemorrhagic strokes in the first 2 weeks postpartum. This observation informed her supplemental study into preeclampsia as related to the maternal neurovascular unit. The goal was to develop and pilot two clinical protocols to prevent neurological SMM and mortality, including postpartum stroke.

Aim 1 of the study was to (a) assess knowledge gaps among OB providers about warning signs of neurological SMM and MM and (b) develop a maternal stroke bundle to be used in the inpatient or emergency/triage setting to ensure that peri- and postpartum women with neurological symptoms receive appropriate evaluation.

Dr. Miller reported on Aim 1(a) results. A survey of 40 OB and emergency department providers to determine their knowledge and comfort with maternal neurological emergencies (MNEs) revealed that 40% had slight or no confidence managing MNEs. More than half did not know

that postpartum was the highest-risk time period or that tissue plasminogen activator, a thrombolytic agent that breaks down blood clots to restore blood flow in acute ischemic stroke, could be given in pregnancy, and only 20% correctly identified all the red flag features of headache. Nearly all (95%) agreed that developing institutional protocols for MNEs in pregnant and postpartum women was important. For Aim 1(b), the investigators developed maternal stroke prevention and treatment educational material in collaboration with the Obstetric Life Support consortium, to be published in the form of a manual. They also created a mnemonic for knowing when a headache is an emergency situation: **SCANME** (Sudden/Severe/Seizure, Change in position of quality, Altered mental status, Neurological deficits/Nausea and vomiting, Medications without relief, Elevated blood pressure or temperature).

Aim 2 of the study was to (a) develop a protocol for near-infrared spectroscopy (NIRS)–based bedside monitoring to identify impaired cerebral autoregulation in women admitted to the hospital with postpartum preeclampsia and (b) pilot the protocol in 10 patients with high-risk neurological features, such as headache.

Dr. Miller reported on the Aim 2(a) results. The investigators wanted to develop a way to identify perfusion problems in the maternal brain when women were admitted with postpartum preeclampsia or a hypertensive emergency. The investigators assembled an apparatus that was basically a portable, NIRS-based cerebral oximetry monitor with continuous, noninvasive blood pressure monitoring. They tested the feasibility and refined the protocol to increase comfort and tolerability, based on feedback from three study participants. Dr. Miller noted that people having this kind of monitoring are usually unconscious, so comfort is a significant factor for using this device on people who are conscious but feeling unwell.

Dr. Miller predicted an exciting future for the field she calls “neuro-obstetrics,” a cross-disciplinary field that goes from bench studies of such things as the blood–brain barrier in pregnant and postpartum people to public health and medical education, collaborating on clinical care, and the bioengineering of new machines.

### *Discussion*

*Please provide more information about cerebral oximetry.* **Dr. Miller** said that cerebral oximetry is often used by neuro-anesthesiologists and in neurocritical care. Patients are usually unconscious when it is applied. The mechanism, which is basically just a sticker taped to the head, monitors the tissue oxygenation index, which is the ratio of deoxygenated hemoglobin to total hemoglobin and is a proxy for cerebral blood flow. It is not perfect, but it is easy to use and does not require a lot of expertise. Dr. Miller noted that in her study, where patients are awake, the headband of her apparatus has been modified to be soft and comfortable.

*Does skin tone affect the cerebral oximetry measurement?* **Dr. Miller** said it does not, nor does skull thickness or many other physiological factors. This is important because maternal stroke, intracerebral hemorrhage, and other complications disproportionately affect people of color. The question illustrates the need for objective criteria to help providers manage and prevent—or at least mitigate—the effects of these devastating complications and not simply send people with a headache home.

*Has the contribution of the maternal immune system been explored in maternal stroke?* **Dr.**

**Miller** said her K23 study is looking at whether neuroinflammation is a significant contributor to neurovascular unit dysfunction in preeclampsia.

## **Presentation: Preconception Contributors to Severe Maternal Morbidity in Black and White Women**

*Janet Catov, Ph.D., M.S., University of Pittsburgh*

The rates of SMM are increasing, and there are profound disparities across all racial and ethnic groups. Among pregnancy-related deaths from 2014 to 2017, 42% to 62% appear to be related to cardiovascular events. This study, a supplement to a parent study looking at life course approaches to cardiovascular risk factors associated with adverse pregnancy outcomes, aims to examine the pre-pregnancy antecedents to SMM events and the associated racial disparities. The hypothesis is that poor cardiovascular health and adverse psychosocial stress before pregnancy contribute to SMM and racial disparities.

The study used data from the NHLBI Coronary Artery Risk Development in Young Adults (CARDIA) study to look at nearly 1,392 women (51% Black) with 2,3720 post-enrollment births for up to 1 year post-delivery. SMM was characterized using the CARDIA study criteria, which included delivery records and self-reported hospitalizations up to 1 year post-delivery. Cardiovascular health (CVH) and stress before pregnancy were also assessed. Self-reported adverse pregnancy outcomes (APOs) were defined as hypertensive disorders, preterm birth, and gestational diabetes. Generalized linear mixed models related CVH and stress to risk of SMM birth were adjusted for race, age, education, parity, and APOs, using non-SMM births as the referent. The 1-year follow-up data from self-reported hospitalizations was divided into SMM in the first 6 weeks after delivery (i.e., hemorrhage, sepsis, cardiomyopathy, and hysterectomy) and SMM events over the entire 1-year period (i.e., cardiovascular events, depression, domestic violence, and overdose).

Dr. Catov said the pre-pregnancy CVH data on risk factors (e.g., age, education, blood pressure, smoking, cholesterol level) did not indicate any racial differences in the occurrence of SMM between Black and White women; overall, the incidence of SMM was similar for both races (1.7% in Black women and 1.9% in White women). However, when the data were aggregated into a pre-pregnancy CVH score as related to SMM and race, Black women in general had worse CVH than White women did, with or without SMM. The investigators used clinical cut points to identify poor, intermediate, or high CVH and found that none of the Black women with SMM ( $n = 19$ ) scored in the high CVH category, compared with about 40% of the White women with SMM ( $n = 24$ ). More than 40% of Black women with SMM scored in the poor CVH category, compared with well under 10% of White women with SMM.

The markers of stressful life events before pregnancy indicated that Black women with SMM were more likely than either Black or White women without SMM to have experienced stressful events. When the pre-pregnancy CVH and stress data were combined and modeled to look at pre-pregnancy health and SMM, there was only a very weak correlation between CVH and stress. However, CVH was found to be highly protective against risk of SMM events in Black women but not in White women. The stress data were less precise. The risk of SMM appears to be modestly higher in Black women who have higher pre-pregnancy stress, but more work is needed to determine what, if any, differences there are between Black and White women.

Dr. Catov summarized the study conclusions:

- Better pre-pregnancy CVH was associated with reduced risk of SMM in Black but not White women.
- Pre-pregnancy stressful life events were more common in Black compared with White women and appeared to have a stronger but not statistically different association with SMM risk.
- Poor pre-pregnancy CVH was associated with risk of SMM in Black women, and pre-pregnancy stress was also linked to SMM.

### *Discussion*

*How was “stressful events” defined, and did it take into account structural racism and SDOH?*

**Dr. Catov** said the CARDIA study began in the mid-1980s and enrolled participants who were in their 20s. It was not possible to disentangle stressful life events around racial or sexual discrimination during the 1980s, from information on the CARDIA questionnaire. The other items that are in the stressful life event category broadly relate to such things as witnessing or being a victim of violence, living in poverty, and having parents who divorce.

*What explains the finding that better pre-pregnancy CVH lowers the risk of SMM in Black but not White women?* **Dr. Catov** suggested that Black women might be more heavily burdened by poor pre-pregnancy CVH than White women, so the lessening of the risk was more pronounced for Black women. Pre-pregnancy CVH does matter for White women, particularly at younger ages, but the burden appears greater in Black women. It would be good to replicate this finding with a more contemporary cohort if preconception data are available.

## **IDENTIFICATION AND PREVENTION OF MATERNAL MORBIDITY AND MORTALITY RISK**

### **Moderator**

*Sarah Yoon, Ph.D., RN, National Institute of Nursing Research, NIH*

### **Presentation: Maternal Obesity and SARS-CoV-2: Maternal Blood and Fetal Placental Immune Response**

*Andrea Goldberg Edlow, M.D., M.Sc., Harvard Medical School*

Pregnancy is associated with a significantly increased risk for SMM and mortality in the context of COVID-19. Pregnant patients with COVID-19 are more likely than nonpregnant patients of the same age to be admitted to the intensive care unit, to receive invasive ventilation, and to die. Recent data showed that SARS-CoV-2 was associated with an increased risk of severe obstetric morbidity and mortality, primarily related to hypertensive disorders of pregnancy, postpartum hemorrhage, and infections other than SARS-CoV-2.

Obesity is a risk factor for severe disease in pregnancy. CDC studies showed that pre-pregnancy obesity, defined as a BMI of 30 or more, was associated with a 1.4-fold relative risk of severe disease. A recent review of more than 63 observational studies showed that one-third of pregnant women hospitalized for COVID-19 had obesity

Dr. Edlow said that the underlying mechanisms that drive the increased risk of SMM in the setting of obesity are not known. She described her study, which has two objectives:

- Determine how maternal obesity alters the maternal cellular (monocyte and T-cell) response to SARS-CoV-2. The hypothesis is that maternal obesity primes T cells and monocytes toward an inflammatory phenotype, resulting in increased pre-inflammatory cytokine production in the context of SARS-CoV-2.
- Determine how SARS-CoV-2 affects the fetal placental macrophage (Hofbauer cell) single-cell transcriptome. The hypothesis is that even in the absence of placental infection, maternal SARS-CoV-2 infection will alter the Hofbauer cell transcriptome.

To evaluate the maternal immune response to SARS-CoV-2, the investigators started with 110 pregnant individuals (36 COVID-19–negative controls and 74 participants with COVID-19). These participants were recruited before vaccines were available, so all were unvaccinated. They were divided relatively evenly between patients with obesity (i.e., BMI  $\geq$  30) and without obesity. The investigators also recruited a competitor group of 45 nonpregnant women of reproductive age (19 COVID-19–negative controls and 26 participants with COVID-19). This group was also divided between lean participants and those with obesity. Peripheral blood mononuclear cells and plasma were isolated from the participants. Cytokine expression was quantified for monocytes, T cells, and maternal plasma. Stool samples from many of the participants were also collected and are being sequenced to determine how the maternal gut microbiome might influence the immune response to SARS-CoV-2 and whether there is directional crosstalk.

The investigators found that monocytes from healthy pregnant women were more reactive than those from nonpregnant controls. Pregnant controls had more pro-inflammatory cytokine production from their monocytes upon stimulation with lipopolysaccharide (LPS). As COVID-19 severity increases, monocytes either are exhausted and can no longer produce pro-inflammatory cytokines in response to LPS or are potentially suppressed. It is not clear whether this is reflective of more pro-inflammatory cytokine production during the illness or whether this potential suppression could itself be driving the pathophysiology. A similar effect has also been observed in nonpregnant populations and across participants both with and without obesity. Dr. Edlow noted that although monocyte exhaustion increases with increasing COVID-19 severity in pregnancy, some recovery of the monocytes' pro-inflammatory capabilities was seen during convalescence. The investigators also found that maternal obesity is associated with a pro-inflammatory CD4<sup>+</sup> T-cell phenotype in COVID-19. The CD4<sup>+</sup> T-cells of pregnant women with obesity produced significantly more IL-2, IL-4, and TNF- $\alpha$ , an increase not seen in the nonpregnant population. A similar pattern was seen with the CD8<sup>+</sup> T-cell phenotype.

To evaluate the fetal placental macrophage single-cell transcriptome, single-cell RNA sequencing (scRNA-seq) was performed on Hofbauer cells that were isolated from homogenized placental villous tissues from 12 placentas (from 4 SARS-CoV-2–positive pregnancies and 8 negative controls). Differentially expressed genes were identified with a negative binomial test, and functional analyses were performed to understand what these genes might be doing. The idea was to use fetal placental macrophages as a surrogate for fetal brain microglia, because they both share a common yolk sac origin. Microglia are largely inaccessible during fetal life and after birth, so this is an opportunity to find a more accessible cell type with a common origin to provide information about the programming effects from various maternal exposures, including obesity, on fetal microglia. The investigators found that

the scRNA-seq demonstrated that COVID-19 was associated with a distinct fetal placental macrophage signature, with more than 1,400 differentially expressed genes in Hofbauer cells in the setting of maternal COVID-19. No placentas had a detectable SARS-CoV-2 viral load. Functional analysis of the differentially expressed genes suggested that maternal COVID-19 was associated with altered Hofbauer cell pro-inflammatory and mTOR signaling, mitochondrial dysfunction, and cell death.

Dr. Edlow summarized the study conclusions:

- Increased pro-inflammatory potential of CD4<sup>+</sup> and CD8<sup>+</sup> T-cells in pregnancy in patients with obesity may help elucidate the increased risk for SMM.
- The significant impact of maternal COVID-19 on fetal placental macrophages suggests fetal immune effects even in the absence of vertical transmission.

Dr. Edlow said future research will focus on developing cellular models for fetal brain cells (microglia) using more accessible proxy cell types in humans, including cord blood monocytes and Hofbauer cells isolated from the placenta.

### *Discussion*

*Since the level of monocyte expression might differ by infectious stage, when were blood samples collected in terms of early or late COVID-19 stage?* **Dr. Edlow** said the blood samples were collected when the participants were hospitalized for illness. The investigators were selecting for people who were symptomatic or admitted for COVID-19, and all blood samples were obtained before the initiation of any treatments or therapies, especially dexamethasone, which could be relevant for monocyte depression. The convalescent samples were usually from the same individuals who had recovered from COVID-19 or from the pregnant population when they went on to delivery.

*Are you also hypothesizing that the Hofbauer effects are indicative of maternal glial cell effects and perhaps some of the postpartum hemorrhage outcomes that are being reported?* **Dr. Edlow** said the hypothesis is that the Hofbauer cell would be more reflective of the fetal brain microglia transcriptome, not the maternal one, because that is where the common yolk sac origin and common programming influence might occur.

### **Presentation: LINK MOMS: Addressing Maternal Morbidity and Mortality in Community Health Centers**

*Sadia Haider, M.D., M.P.H., Rush University; and Rachel Caskey, M.D., M.A.P.P., University of Illinois at Chicago*

Dr. Haider said the LINK MOMS study is a collaboration among co-investigators at AllianceChicago, an organization dedicated to improving personal, community, and public health through a network of community health centers (CHCs). AllianceChicago has 74 CHCs spanning 20 states and clinical data on nearly 4 million patients.

LINK MOMS is a supplement to a parent study looking at how to improve maternal outcomes by ensuring a continuum of care throughout pregnancy and removing barriers to timely access to postpartum contraceptive care by linking the mothers' care with the well-baby visits. The LINK MOMS study uses a population-based approach to identify the health outcomes of a

defined group of people. For LINK MOMS, this involves identifying the clinical, social, economic, and behavioral factors associated with adverse outcomes for pregnant and postpartum people in order to create a registry that identifies pregnant and postpartum people at risk and facilitates earlier connections to care. This timely access to care could be a critical preventive measure for SMM and maternal mortality. LINK MOMS has three aims:

- Aim I: Build a population health interface to identify pregnant and postpartum people at risk for SMM or maternal mortality, using standard clinical data from electronic medical records (EMRs), and create a LINK MOMS registry.
- Aim II: Validate the LINK MOMS registry, using data from CHCs across the country.
- Aim III: Design an implementation plan for the LINK MOMS registry in the CHCs.

The study uses the Health Catalyst Population Builder platform to identify the patients meeting the criteria for specific conditions that could result in poor maternal health outcomes.

Dr. Caskey reviewed the study outcomes to date:

- Aim I: The investigators have conducted two sessions with subject matter experts, reviewed transcripts of those sessions for key variables for identifying people at risk for SMM and maternal mortality, and explored documentation practices at CHCs to identify which key variables were most frequently used. Key variables included gestational diabetes, depression, multiple gestations, smoking, maternal age, domestic violence, and hypertension.
- Aim II: The Population Builder tool was applied to build the registry, which was informed by the list of variables. Out of almost 4,000 unique patients in databases from five CHCs, nearly 3,000 patients were identified as being positive for at least one variable. Validation of the registry's accuracy in identifying people at risk of SMM and MM is in progress. The investigators are developing an abstraction tool to standardize the chart review process and a scoring system to stratify patients by risk level.
- Aim III: The investigators will be conducting interviews with moms to get their feedback on their care needs, the LINK MOMS registry itself, and their suggestions for how the registry should be used and whether there are privacy concerns. Interviews with providers will focus on clinicians' preferences for utilization of registry data in clinical practice, barriers and facilitators to using the registry, and any resource issues.

Future directions include testing the registry in AllianceChicago CHCs across the country and following the outcomes longitudinally, broadly sharing findings and data points that are predictive of high risk of SMM and MM, allowing the LINK MOMS validated approach to be used by other clinical care settings and their EMR systems, and seeking further funding for an implementation trial of the LINK MOMS registry.

## Discussion

*How did you educate the lay stakeholders so they felt comfortable with their role on the research project?* **Dr. Caskey** said the stakeholders come from very different backgrounds and include clinicians and other professional stakeholders, as well as lay stakeholders and patients.

It was important to emphasize all of the stakeholders' importance to this process and to make clear that if something does not make sense to pregnant people, the work is in vain.

*Will the Population Builder be part of the EHR system?* **Dr. Caskey** said it would. It essentially extracts data from a patient's EHR. The idea was to create a tool that flags certain identifiers for adverse pregnancy outcomes within an EHR. Sites can decide how to act on those data, such as identifying people most at risk or by identifying patients based on specific risk factors.

*Are the key risk factors you are identifying a combination of SDOH and clinical factors?* **Dr. Haider** said they are. The goal is to balance how much is put into the tool to make it practical and useful for the health centers, so there must be the right balance between clinical and social factors. SDOH factors are just as important in predicting outcomes, but one of the biggest challenges is how or whether SDOH are documented in the EMRs.

Universal SDOH screening and documentation is important and should be part of the patient's EHR during prenatal care. **Dr. Haider** agreed. Improving SDOH screening and documentation would make the tool more valuable.

### **Presentation: Is Maternal Risk-Appropriate Care Associated with Decreased Severe Maternal Morbidity for Abnormal Placentation? Preliminary Results of a Mixed Methods Study**

*Kimberly Gregory, M.D., M.P.H., Cedars-Sinai Medical Center*

Dr. Gregory said that although maternal mortality is increasing in the United States, it is decreasing in California, possibly due to the widespread implementation of hypertension and hemorrhage bundles. However, SMM is still a significant problem in about 3% of all pregnancies. CDC lists 21 conditions of SMM, but that list includes disseminated intravascular coagulation and shock, which are potentially preventable, and hysterectomy and transfusion, which are actually part of the treatment for SMM. Dr. Gregory suggested that it might not be fair to include these treatments and preventable conditions in the definition of SMM. Ventilation is also listed, even though many patients prefer to have general anesthesia for procedures.

Dr. Gregory noted that a series of papers had outlined the criteria for "accreta centers of excellence." She described three abnormal placentation conditions: placenta accreta spectrum disorder (PAS), a potentially fatal condition associated with significant hemorrhage, which can require transfusion and/or hysterectomy; placenta previa, which requires cesarean delivery, with increased risk of bleeding, transfusion, and hysterectomy; and low-lying placenta, for which cesarean delivery is often recommended due to an increased risk of bleeding. Dr. Gregory said her study aimed to identify the policies and procedures in place at high-volume centers in California over a 2-year period to determine the extent to which maternal outcomes were associated with the volume of hospital procedures, specific services that were provided, and the hospital's maternal level of care designation, if it had one.

Of the more than 1.3 million deliveries in California from 2016 to 2018, 1,677 (0.12%) were cases of placenta accreta, and 11,146 (0.82%) were cases of placenta previa. The hospitals designated as accreta hospitals, which represent 25% of all hospitals, saw nearly half of the accreta cases and one-third of the previa cases, suggesting some type of informal triage and

regionalization of care for these disorders. During this time period, out of 196 birthing hospitals, 27 were considered high-volume centers (i.e., at least six placenta accreta cases per year).

The investigators conducted structured interviews with the chief of obstetrics or a designee at 20 of the high-volume hospitals to determine what resources and services should be available in accreta centers. The investigators found considerable variation among the hospitals. A majority of the hospitals performed preoperative hemoglobin optimization; had a designated accreta team; routinely placed an arterial line; had access to an in-hospital blood bank, a cell saver, and perfusionists; and had a massive transfusion protocol. But only about half performed a confirmatory magnetic resonance imaging (MRI) scan, admitted patients in advance for preparation with a special team, routinely placed a central line, had access to interventional radiology, did cystoscopy and stent placement before surgery, had a preoperative plan for going directly to a cesarean hysterectomy, or did a formal debriefing after the procedure. The number of physicians on the accreta teams ranged from 1 to 15. Only 13 (65%) of the hospitals considered their institution to be a designated accreta center.

Dr. Gregory summarized the interview responses, noting that almost all centers had a multidisciplinary team headed by a maternal–fetal medicine (MFM) specialist and a skilled surgeon and had massive transfusion protocols. Centers varied with regard to intraoperative monitoring, preemptive prophylactic procedures, number and types of surgeons, and placental removal and planned cesarean hysterectomy. Primary surgeon expertise ranged from OB/GYN specialists, to MFMs, to gynecological oncologists. Hospitals generally described their outcomes as “excellent,” citing low rates of transfusions, sending the majority of women to the regular postpartum floor after the procedures, and not requiring a hysterectomy or interval procedure as successful outcomes.

Dr. Gregory said conducting the interviews herself gave her insight into the following recommendations for future study, which are based on what some of the centers are already doing:

- Require consensus of two-thirds of MFMs on ultrasound readings before proceeding with a hysterectomy; otherwise, just attempt to remove the placenta.
- Encourage more active interaction between accreta nurses and the patient and family throughout the hospital stay. Involve social workers or psychological consultations to address post-traumatic stress syndrome.
- Provide a debriefing that includes the patient.
- Institute monthly conferences to compare specimens with ultrasound or MRI in the presence of both the surgeon and the imaging consultant.
- Use suture ligation for bloodless hysterectomy.
- Conduct immediate preoperative ultrasound for instant feedback to confirm false positives.
- Perform cystoscopy after delivery if the bladder is involved, and leave the placenta in

until patient returns in 6 weeks.

- Conduct annual simulations with the team.

Dr. Gregory outlined some next steps:

- Stratify hospitals by policies and procedures and evaluate maternal SMM outcomes by both including and excluding hysterectomy and transfusions. Excluding hysterectomy and transfusions would likely provide a different metric of SMM for PAS.
- Determine whether there are disparities in outcomes by race and ethnicity for the placental conditions, stratified by policies, procedures, and sites.
- Share descriptive summary results with study participants, who exhibited interest in what other hospitals were doing during the interviews.
- Propose a quality metric to determine how well the different centers are managing the placental conditions. The current measure of SMM does not capture that metric. Consider developing a patient registry.
- Determine which policies and procedures should be universal for optimum outcomes across all sites.

### *Discussion*

*Is there any geographic variability (e.g., rural or urban) or resource availability associated with the outcomes?* **Dr. Gregory** said the hospitals were spread across California, with some regional centers in more rural areas that smaller hospitals refer to. The biggest difference was the subspecialty of the primary surgeon. In the less urban, less academic centers, the primary surgeon was more likely to be a generalist and the team would be smaller. But often, the more rural the site, the more dedicated the team.

*Why does accreta require surgery, which seems extreme?* **Dr. Gregory** said the consensus of the centers of excellence was to proceed directly to a planned cesarean hysterectomy to reduce overall blood loss and morbidity. But not all centers do this, and other sites advocate for hysterectomy to be a patient-centered decision, although that means accepting the possibility of increased morbidity.

*Is MRI, which may not be available in all centers, required for a diagnosis?* **Dr. Gregory** said there is no consensus that MRI is needed, but there is a consensus that it should be available.

## **STRUCTURAL AND SYSTEMATIC CONTRIBUTORS TO MATERNAL MORBIDITY AND MORTALITY**

### **Moderator**

*Jennifer Alvidrez, Ph.D., Office of Disease Prevention, NIH*

### **Presentation: Affordable Care Act (ACA) Medicaid Expansion and Maternal Morbidity**

*Pinka Chatterji, Ph.D., University at Albany*

Dr. Chatterji said that U.S. SMM rates, which are higher than in similar industrialized countries, have been rising in recent years. There is growing evidence that preconception health is an important factor in determining pregnancy and childbirth outcomes. Medicaid, which financed

about 42% of all U.S. births in 2018, covers eligible mothers from conception to 60 days postpartum. However, beginning in 2014, a majority of states and the District of Columbia expanded Medicaid income thresholds to include more low-income adults, including those without minor children. Although the expansion did not target pregnant women, it led to women having more access to expanded insurance and more opportunities for preconception and post-delivery coverage.

As part of a larger study on the effect of state policies and educational attainment on U.S. adult mortality risk, this research supplement aimed to examine whether Medicaid expansion enacted under the Affordable Care Act (ACA) was associated with maternal health outcomes and behaviors among women ages 21 to 55 and whether there were differential effects based on maternal age, with a focus on older mothers ( $\geq 35$  years old), who are at an elevated risk for maternal morbidity and mortality. The study used a difference-in-differences approach to compare mothers living in states that expanded Medicaid versus adults without minor children and mothers living in states that did not expand Medicaid, to compare outcomes both before and after the expansion. Data were gathered from birth certificates and state-level rates of SMM. The sample was limited to first births to allow for the examination of exposure to Medicaid expansion among those not already Medicaid eligible. Outcome variables were health problems defined as those occurring before or during pregnancy (e.g., hypertension, pre-pregnancy or gestational diabetes, eclampsia) and those occurring at delivery (e.g., maternal transfusion, ruptured uterus, unplanned hysterectomy). Individual covariates included age, marital status, race, and cesarean section. County-level covariates included percent unemployed, per capita income, percent in poverty, health professional shortages, number of bassinets, and number of OB-GYN specialists.

Dr. Chatterji summarized the results:

- In looking at the means of the outcome variables, investigators found that health problems occurring before and during pregnancy were common, and rates were higher for mothers in the older group (25.7%) than in the younger group (14.2%). Health problems occurring during delivery were rare and occurred at similar rates in both groups.
- In 2011 and 2012 (prior to the Medicaid expansion), there were no differences between the mothers in the states being studied. After the expansion, there was a significant increase in identified health problems in 2014 and 2015 among mothers in the expansion states before and during pregnancy, but these numbers declined from 2016 to 2018. Medicaid expansion appeared to be associated with an increase in health problems during delivery for both younger and older mothers, but levels remained high for older mothers while decreasing from 2016 to 2018 for younger mothers. The reasons for this surprising finding are not clear, though it is possible that Medicaid expansion led to greater identification of problems rather greater incidence of problems. No effects of the Medicaid expansion were seen on state SMM levels.

Dr. Chatterji said that although the preliminary findings of the study suggest that the ACA expansion of Medicaid may have increased identification of health problems before and during pregnancy in both younger and older mothers, an investigation of mechanisms is needed,

because the study did not find consistent effects on maternal health behaviors, including use of prenatal care. The role of non-Medicaid subsidized insurance, including Marketplace subsidized plans, should also be examined. Moreover, the mixed findings between younger and older mothers experiencing problems during delivery were surprising and are difficult to explain. Investigators may want to explore whether Medicaid expansion might have affected the composition of mothers or affected the supply of providers.

### *Discussion*

*Did the study look at interactions, such as race and ethnicity by age?* **Dr. Chatterji** said that is the next area for investigation. The huge sample from birth certificates makes it possible to look at, for example, race and education subsamples. One limitation is that the data have already been aggregated at the state level.

*What is the quality of SMM data? It seems underestimated.* **Dr. Chatterji** agreed that that is a concern. The SMM data are based on the International Classification of Diseases (ICD) codes, which are predicated on the procedures and diagnosis during delivery. This is essentially the list of conditions from CDC. A complicating factor that also must be taken into account in the analysis is that the quality of the data may be changing over time in different states.

*Expanding access to Medicaid and facilitating people signing up for Medicaid are two different things. Has that played a role in seeing an increase in identified health problems early on but not later?* **Dr. Chatterji** said this would be a good question to address. She noted that the mother's insurance status is on the birth certificate, but many mothers get signed up for Medicaid late in the pregnancy or at the time of delivery, so that information may not be very helpful. However, there are other datasets that include information on the mother's insurance status before and after giving birth, and other researchers are looking at that.

### **Presentation: Mitigating the Impact of Implicit Bias on Maternal Morbidity and Mortality for African American Women**

*Gwendolyn Norman, Ph.D., M.P.H., Wayne State University and Sarah Blake, Ph.D., M.A., Emory University*

This research is a collaborative effort between cohorts in Detroit, Michigan, and Atlanta, Georgia, as a supplement to a parent NIH grant, "Environmental influences on Child Health Outcomes (ECHO)," with the goal of expanding the focus to maternal mortality through the voices of women. Because it plays a role in pregnancy outcomes, implicit bias has become a target of research. A 2003 Institute of Medicine report identified attitudes and behaviors of healthcare providers as factors that contribute to health disparities. The report suggested that unrecognized bias against racial and ethnic minorities might significantly affect communication and receipt of care, particularly as related to patient-provider interactions, provider treatment decisions, patients' adherence to treatment, and health outcomes.

The Detroit and Atlanta ECHO groups have worked together to develop guides for focus groups and interviews to help elucidate the experiences of Black women when seeking care across the pregnancy spectrum. The guides address structural and social barriers to achieving racial equity in healthcare services. The groups have also co-created interview guides for healthcare providers to gauge their knowledge of the role of implicit bias and racism in the prenatal,

delivery, and postpartum care of Black women.

Dr. Norman, a co-investigator for the Detroit ECHO cohort, said her cohort is focusing on reducing maternal morbidity and mortality through a study that captures the voices of women and their healthcare providers. The team is collaborating with the Southeast Michigan Perinatal Quality Improvement Coalition (SEMPQIC), a group that works to improve birth outcomes by engaging a wide variety of community and clinical stakeholders. The goal of the study is to identify interventions to reduce the impact of bias in healthcare that may contribute to increased risk for maternal morbidity and mortality in high-risk populations. The study engages Black mothers, community advocacy organizations, and healthcare providers in structured interviews and focus groups. The data will be used to develop a toolkit of specific strategies for mothers to counter negative interactions and obtain patient-centered, respectful care. The first phase of the study, which began in June 2021 and has resulted in numerous provider and maternal interviews and focus groups, will identify facilitators and barriers for mitigating the impact of implicit bias and racism in this healthcare setting. A second phase will develop the strategies needed to optimize healthcare services for Black mothers.

Dr. Blake, a co-investigator for the Atlanta ECHO cohort, noted that Georgia has some of the highest rates of maternal mortality, with Black women experiencing 1.6 times more maternal deaths than White women. This imbalance requires critical examinations of maternal health disparities. The Atlanta ECHO project seeks to address the impact of exposure to systemic racism and implicit bias on the mother during the pre-, peri-, and postnatal periods; Black women's experiences with implicit bias and racism in healthcare; and critical strategies for reducing or mitigating the effects of these exposures on the health of Black mothers and their families. The study is being conducted in collaboration with the Center for Black Women's Wellness (CBWW), which has assisted with the development of data collection instruments, recruitment, and provider interviews and focus groups.

Dr. Blake noted that providers might believe they have made the best medical decisions for their Black patients but be unaware that their decisions were distorted by implicit bias. The hypothesis of the study is that eliciting guidance from Black women and their healthcare providers, through the lens of reproductive justice, respectful care, and health equity, can offer important information to improve the treatment of Black women in the healthcare setting. The aims and methodology of the Atlanta study are similar to those of the Detroit cohort. Dr. Blake outlined some of the key interview areas for providers in (e.g., their observations of rationing treatment due to race or ethnicity, their beliefs about Black women's experiences of implicit bias, their own experiences with provider training to address equitable care and implicit bias) and shared some of the preliminary themes from the interviews:

- **Impact of bias on clinical care:** Providers acknowledged that implicit bias may play a role in their own care of Black women and said they had witnessed such clinical bias on the part of colleagues.
- **Stressors and weathering effects on Black women:** All providers recognized that Black women experience lifelong stress due to racism and discriminatory treatment, but few reported knowing how to address this in their clinical care of Black women.

- **Respectful care:** Providers defined respectful care for Black women in a variety of ways, such as listening to their patients and acknowledging their concerns.
- **Equitable care:** Providers defined equitable care for Black women as providing the same standards of quality maternal healthcare. They suggested strategies to ensure equitable care, such as providing patient-centered care and addressing their own biases.

Next steps will include sharing additional and important findings from the voices of Black women with their study colleagues at CBWW and using these data to work toward solutions for reducing implicit bias and achieving respectful and equitable care.

### *Discussion*

*Were there differences in implicit bias among different types of providers, such as doulas compared with physicians?* **Dr. Blake** said her group did not interview doulas. However, among the physicians and nurse midwives who were interviewed, there was recognition of implicit bias and similar definitions of equitable and respectful care. The nurse midwives offered more strategies for addressing implicit bias. This illustrated the importance of training and the need for additional exposure to these issues across hospital systems. **Dr. Norman** said the doulas her group interviewed did not perceive implicit bias from others in their field but did observe it in the delivery suite with other providers.

*How representative were the clinicians who were interviewed? Were those with more cultural sensitivity or cultural humility more likely to participate in the interviews?* **Dr. Blake** said almost all of their providers had some exposure to training, although they varied in their views about the value of additional training, suggesting that hospital-based culture change was required. The next phase of the study will include developing a higher-level implicit bias training.

*How is explicit bias, not just implicit bias, taken into account?* **Dr. Norman** said providers would sometimes voluntarily mention that they had seen explicit bias, and that is being analyzed.

*Was there a difference by age regarding perceptions of bias among both providers and patients?* **Dr. Blake** said patient participants ranged in age from 19 to late 30s, so a “generational” difference will be considered. Providers were about the same age. She added that certified nurse midwives tended to be more descriptive about bias and mitigation strategies.

### **Presentation: A Public Health Exposome Approach to Maternal Mortality**

*Emily Harville, Ph.D., Tulane University School of Public Health and Tropical Medicine*

This study is a supplement to a parent grant that aims to identify social contexts (e.g., structural racism, violence, income inequality) that increase risk for pregnancy-related mortality and pregnancy-associated homicide. The supplement aims to develop models incorporating individual- and environment-level predictors of maternal mortality for the United States as a whole and for Louisiana in particular, using an exposome-wide computational approach. This work involves considering every maternal death as part of and inseparable from the context in which it occurs. The project seeks to identify possible points of intervention that include the places where women are born, live, and work; the policies that shape those places as either protective of or harmful to health; and the societal structures that dictate the distribution of

power and health.

Dr. Harville said the study uses the Public Health Exposome (PHE), a data source containing more than 62,000 variables that have been geocoded and harmonized at an annual and county level, with 6,500 of the variables dating from 2014 to 2018. The variables comprise five overlapping domains: natural (e.g., climate, weather, chemical exposures), built (e.g., land use, building, transportation), social (e.g., demographics, economic systems), policy (e.g., government expenditures, benefit programs), and health (e.g., healthcare availability, health outcomes). The hypothesis is that being exposed to all these domains over time affects the risk of death during pregnancy and the postpartum period and that differential exposures to this exposome produce maternal population health inequities.

The study used data on pregnancy-related deaths from 2015 to 2018 from the National Center for Health Statistics at the national and county level and the linked vital records data with verified maternal deaths from 2016 to 2018 for Louisiana (i.e., individual-level data). Dr. Harville gave a simplified overview of the high-dimensional computational methods needed to study such complex variable relationships. The toolchain starts by harmonizing the heterogeneous raw data and identifying groups that have maternal mortality. A subset of the variables that are considered important is extracted from these groups, after which traditional statistical methods can be applied.

Three county-level factors that were direct upstream predictors of maternal mortality rates were overall years of potential life lost, lack of physical activity, and extreme heat. In an unsupervised analysis, the paraclique or cluster contained all the maternal mortality variables, as well as the race- and ethnicity-specific variables coming from all of the PHE domains. Dr. Harville said results from the national-level PHE data could be applied to the individual-level Louisiana data, with some additional controls for confounding. For example, sun exposure, which was modestly correlated with pregnancy-related mortality at the national level, was much higher in Louisiana. When national ecologic results were applied to individual-level data, preliminary findings confirmed pregnancy-related mortality associations with years of potential life loss and a healthy food environment. Dr. Harville noted that limitations when working with a national dataset include the need for ecological correlations, the small number of maternal deaths, autocorrelated variables in the dataset, and the limited number of some exposures, particularly in the policy environment.

Dr. Harville presented the following conclusions:

- Contextual factors, such as poverty, that predict general health also predict maternal mortality.
- Maternal mortality correlates with overall population health and disability—it is not a separate issue.
- Data-driven computational methods can be helpful in addressing real-world complexity. Methods and analytics that can be applied to large, complicated datasets are needed.
- Results from many different data sources indicate the need for comprehensive and multidisciplinary work to address the problem.

## Discussion

*How can the findings from these computational models be translated into policy changes?* **Dr. Harville** said that her results are still preliminary, but looking at factors like poverty helps make it clear that maternal mortality is part of a broader social fabric and must be addressed as a society-wide problem.

*Is there interest in looking at the impact of climate change and maternal mortality, particularly given some factors that seem to be associated with climate?* **Dr. Harville** said the findings about sun and heat exposure were surprising and should be studied more, since they came up several times in the analysis.

*Is this type of research possible in most parts of the country, or does Louisiana have a particular overlap of excellent data sources?* **Dr. Harville** said her work involves a nationwide dataset. In Louisiana, the investigators had access to individual-level data. Most of the variables cover almost all of the country, with the exception of a few of the environmental ones. However, the study did limit the national-level analysis to counties with at least 1,000 births, so there are certain parts of the country that would not have enough people to permit a good analysis. **Dr. Harville** added that she would be happy to hear from investigators in other states who have individual-level data.

*Is there a seasonal pattern to maternal mortality given the extreme heat correlation?* **Dr. Harville** said she did not know.

## Presentation: Understanding Maternal Vitamin D Deficiency in Rural Pregnant Women in South Carolina

*Carol L. Wagner, M.D., Medical University of South Carolina (MUSC)*

Underrepresented minorities, including African Americans, are at greatest risk of vitamin D deficiency and have the highest risk of maternal complications. Vitamin D is a steroid hormone. Unlike other hormones that the body can make endogenously, vitamin D production depends on skin exposure to sunlight. Several studies from around the world suggest that vitamin D supplementation started early in pregnancy and sustained throughout reduces the risk preeclampsia, preterm birth, gestational diabetes, and Cesarean section. Yet despite these emerging benefits, women remain deficient in vitamin D during pregnancy.

In sunny South Carolina, rates of vitamin D deficiency in pregnant women in rural areas have remained largely unchanged since 2010. African American and Hispanic women are the most affected, and virtually all African American infants admitted to the MUSC neonatal intensive care unit have vitamin D deficiency, which in many cases is severe. A vitamin D screening and supplementation field trial conducted from 2015 to 2017 showed that gestational age rose and the risk of preterm birth decreased as vitamin D supplementation increased.

Dr. Wagner said her study, which is a supplement to her community engagement grant, was designed to better understand maternal and healthcare professionals' attitudes and beliefs about vitamin D deficiency during pregnancy in rural South Carolina. Working with two active community obstetrical practices, the investigators aimed to

- Track baseline vitamin D deficiency in pregnant women through EHRs from the

preceding year to document the severity of the problem, rates of vitamin D treatment, and pregnancy outcomes,

- Conduct interviews with providers to understand current strategies implemented by them to monitor maternal vitamin D status during pregnancy, and
- Conduct interviews with pregnant women in two rural communities to determine what intervention strategies would be most effective in achieving vitamin D sufficiency in those at greatest risk.

Qualitative data were analyzed using the constant comparative method. Dr. Wagner reported the study results:

- EHR data were obtained for 822 participants. The majority of participants were African American, had public insurance, and lived more than 10 miles—and, in some cases, up to 30 miles—from a hospital. They had fewer prenatal visits (mean of 10) than the expected 12 to 14 visits during pregnancy. Nearly all had a live birth, but 11% of the infants were preterm, with a gestational age of fewer than 37 weeks. Vitamin D status was measured in only 8.4% of the women; of that group, 57% met the criterion for deficiency. In this cohort of very at-risk women, only 9.1% were prescribed vitamin D supplementation.
- Out of 400 eligible women, only 3 pregnant women participated in the interviews. They said that remembering to take the vitamin D was hard and that they did not see the benefit; only one of the three women felt there was a potential association between low vitamin D levels and prenatal risks. The women described their family members as their most trusted source when making decisions about health during pregnancy.
- Seven physicians participated in the interviews. They said barriers for consistent vitamin D usage included lack of insurance, inability of patients to take pills during pregnancy due to nausea, lack of clarity about the benefits of vitamin D during pregnancy, and lack of access to a local pharmacy. The physicians emphasized the limited standardized protocols for vitamin D usage among pregnant women.

Dr. Wagner summarized the findings of the study:

- EHR data showed that despite the high prevalence of vitamin D deficiency in pregnant women living in rural South Carolina, few are tested and even fewer receive vitamin D supplements.
- Patient respondents were unaware of their deficiency and of the link between vitamin D deficiency and adverse pregnancy outcomes.
- Physician respondents cited conflicting data about when to prescribe vitamin D and noted patients' lack of compliance even with taking prenatal vitamins.
- Access to care affected every aspect of pregnancy outcomes, including vitamin D supplementation. Distance to the hospital was associated with access to care. Less than 50% of the women in these rural areas had access to perinatal services within a 30-mile drive of their homes, and more than 10% drove 100 miles or more for these services.

Dr. Wagner said that improving maternal and fetal health during pregnancy, with a specific focus on maternal vitamin D status, requires understanding the processes involved in diagnosing, treating, and educating pregnant women about vitamin D deficiency and its health effects, particularly in rural and low-resource areas. Education must include public health officials, healthcare providers, and the patients themselves. Limited funding affects dissemination and implementation programs for achieving sustained, positive change.

### *Discussion*

*Would more clear guidance from the American College of Obstetricians and Gynecologists (ACOG) help in addressing some of these disparities?* **Dr. Wagner** said it could be helpful, noting that the last recommendation from the National Academy of Sciences on vitamin D came out in 2011. She suggested that in light of more recent data on vitamin D's effect on immunity, ACOG will likely have a more definitive recommendation.

*Do other countries have more clear guidelines for vitamin D supplementation?* **Dr. Wagner** said they do not. Other countries follow the United States' lead. There are areas of the world where there is a much more profound deficiency, but unlike antibiotics' immediate effects on infections, the effects of vitamin D can be quite subtle.

*Is the high cost of vitamin D testing a barrier, particularly if it is not covered by insurance?* **Dr. Wagner** said South Carolina will pay for any woman who has a risk for vitamin D deficiency that justifies a test, particularly for public assistance patients who are at greater risk.

### **Presentation: Medicaid Expansion and Postpartum Health**

*Claire E. Margerison, Ph.D., Michigan State University*

Federal law requires states to provide Medicaid coverage for low-income pregnant people. This coverage expires 60 days postpartum. Before the passage of the ACA, new parents would have to requalify for Medicaid under parental thresholds, obtain private insurance, or be uninsured. Beginning in 2014, the ACA allowed for expanding Medicaid to all adults with incomes below the federal poverty level. Thirty-seven states and the District of Columbia enacted the ACA Medicaid expansions.

This study, which focuses on the states with Medicaid expansions, is a supplement to the parent grant "Policy Change and Women's Health." The goal is to examine the impact of ACA Medicaid expansion on postpartum insurance coverage, mental health, and pregnancy-associated mortality. The study used two datasets: the Pregnancy Risk Assessment Monitoring System (PRAMS), which provided self-reported Medicaid coverage and postpartum depressive symptoms, and U.S. vital statistics data (i.e., death certificates), which researchers used to assess pregnancy-associated mortality. Dr. Margerison explained that only revised death certificates were used, because they include a pregnancy checkbox to indicate a range of days the person had been pregnant before death (i.e., pregnant at death; not pregnant, but pregnant within 42 days of death; or not pregnant at death, but pregnant 43–365 days before death). The investigators included deaths due to all causes, not just those caused or exacerbated by pregnancy, because in a related study, they had found that more than 20% of pregnancy and postpartum deaths in the United States are due to drug-related causes, suicide, or homicide. The researchers wanted to examine whether mortality occurring in the later

postpartum period after the 60-day post-partum coverage expires, decreased after Medicaid expansion.

Dr. Margerison reviewed the study results:

- No impacts of Medicaid expansion on postpartum depressive symptoms were found.
- No statistically significant associations between Medicaid expansion and pregnancy-associated mortality were found during pregnancy, within 42 days postpartum, or in the later postpartum period, which was when the investigators had hypothesized an association would be seen.
- No significant impact of Medicaid expansion on pregnancy-associated mortality among Hispanic, non-Hispanic Black, or non-Hispanic White people was found, although there appears to be a trend showing that Medicare expansion was associated with a reduction in pregnancy-associated mortality among non-Hispanic Black people. This preliminary finding will be studied further as data become available.

Dr. Margerison summarized the study's conclusions:

- Medicaid expansion in 2014 likely increased Medicaid coverage in the postpartum period.
- No significant impacts of Medicaid expansion on postpartum depressive symptoms or pregnancy-associated mortality were found.
- Insurance coverage alone is likely necessary but insufficient to reduce racial and ethnic disparities in postpartum morbidity or mortality.

### *Discussion*

*Some preliminary findings using PRAMS indicated that 20% to 26% of postpartum people would gain Medicaid, with larger gains for Black and Hispanic people. Retaining Medicaid in the postpartum period (as opposed to losing it) is associated with an increase of 4 percentage points in postpartum check-ups among Hispanic people and a drop of 9 to 12 percentage points in postpartum depressive symptoms only among non-Hispanic White people. What do these findings mean?* **Dr. Margerison** said a number of states are seeking federal waivers to expand Medicaid from 60 days postpartum to 12 months postpartum. Her research found that retaining Medicaid in the postpartum period was associated with an increase in postpartum checkups, but only for Hispanic people; the opposite was true for Black people. Retaining Medicaid was associated with a decrease in postpartum depressive symptoms only among White people. These are preliminary findings with a lot of racial and ethnic differences to be explored.

*Is the population in the analyses from the entire country or from a specific region?* **Dr. Margerison** said it is from the entire United States, but not every state is included, because some states do not participate in PRAMS or do not have the vital statistics data with the necessary data points.

*Although Medicaid expansion did not produce sufficient postpartum improvements, are there other state laws, such as minimum wage, maternity leave, or sick leave policies, that might have*

*an effect?* **Dr. Margerison** said there is room to study the effects of these policies, but her group has not done so yet.

*Has there been an increase in diagnoses of postpartum depression? Have you looked at increased access to postpartum contraception or postpartum well visits?* **Dr. Margerison** said her team can look only at self-reported symptoms, not diagnoses. Contraception has not yet been examined, but it will be.

## MENTAL AND BEHAVIORAL HEALTH

### Moderator

*Lauren D. Hill, Ph.D., National Institute of Mental Health, NIH*

### Presentation: Severe Maternal Morbidity (SMM) in Commercially Insured Individuals

*Kara Zivin, Ph.D., M.S., M.A., M.F.A., University of Michigan*

This study is a supplement to a parent study, “Maternal Behavioral Health Policy Evaluation,” which looks at the impact of policy changes on individuals with perinatal mood and anxiety disorders. The study focuses on SMM in all delivering women (not just those with perinatal mental health conditions) who have been continuously enrolled for one year before and until one year after delivery, and it considers elements of parity laws, including race, ethnicity, and income.

Dr. Zivin reported the results from the first paper to come from the study, “Assess Rates and Characteristics of SMM in Commercially Insured Individuals.” The paper is a comparison of delivery-related early and late postpartum SMM among individuals with commercial insurance in the United States from 2016 to 2017. The investigators separated blood transfusions from other forms of MM, because of the prevalence of SMM related to blood transfusions. The leading causes of SMM during delivery were blood transfusion, hysterectomy, eclampsia, heart failure or arrest, and acute kidney failure. In the periods from discharge to 42 days postpartum and from 43 days to 365 days postpartum, additional causes of SMM were observed, including sepsis and adult respiratory distress syndrome.

The investigators also compared SMM with and without blood transfusions across these same time periods by race and ethnicity and by the presence of perinatal mood and anxiety disorders (PMADs). Black individuals had the highest rates of SMM and PMADs across all three of the time periods, both with and without the inclusion of blood transfusion data.

Dr. Zivin said next steps include assessing the impact of the Mental Health Parity and Addiction Equity Act and ACA implementation on SMM among childbearing individuals with commercial insurance from 2008 to 2019. Preliminary findings suggest a drop in SMM, especially among those with PMADs. Other potential investigations include examining the effect of SMM on infant outcomes and comparing findings from commercially insured populations against a national Medicaid sample.

### Discussion

*It seems that the people who had the most difficulty with PMAD also had other types of SMM. Is there some common variable driving this, or is one causing the other?* **Dr. Zivin** said that it is hard to identify causal connections from the study. There almost seems to be a multiplicative

effect where people who have more conditions coming into the pregnancy experience greater morbidity during pregnancy, but it has not been possible to tease this out. There is a temptation to split out mental health from physical health outcomes, but they can overlap and influence each other.

*Is there a reason for using discharge at 42 days instead of the 60 days of postpartum care currently covered by the ACA?* **Dr. Zivin** said the participants in this study were privately insured, so the Medicaid timing did not apply. Also, the time windows used in the study are those commonly used to categorize SMM.

*Have you looked at the interactions between PMADs and substance use disorders (SUDs), since some of the effects of these two disorders might overlap?* **Dr. Zivin** said the investigators are looking at this interaction.

### **Presentation: Leveraging Technology to Improve Screening, Brief Intervention, and Referral to Treatment (SBIRT) for Pregnant and Postpartum Persons**

*Constance Guille, M.D., Medical University of South Carolina*

One in five women will experience maternal mental health and substance use problems during pregnancy and in the postpartum year. These problems affect not only the person giving birth (e.g., in terms of preterm birth and cesarean sections) but also their children's health (e.g., causing cognitive, motor, and growth delays or behavioral and mental health problems). U.S. Maternal Mortality Review Committees reported that from 2008 to 2017, one in nine maternal deaths was due to a mental health condition, and 100% of those deaths were preventable. Professional organizations recommend screening pregnant and postpartum women for mental health, substance use, and intimate partner violence, doing a brief intervention, and then refer them to treatment (i.e., the SBIRT model). But on a national level, only one in eight women will be screened, and Black people are less likely to be screened than White people are. Similarly, Black women are significantly less likely than White women to access treatment.

Dr. Guille said barriers to SBIRT come from both providers and patients. Providers cite insufficient time, not being familiar with SBIRT, lack of knowledge about mental health and SUDs, and lack of available providers for these conditions. Patients cite the stigma of acknowledging these conditions, fear of legal or social services consequences, and lack of access to care due to transportation, childcare, work, or insurance issues. The barriers were more pronounced for Black women than for White women.

Dr. Guille said her study was designed to leverage technology to overcome these barriers. The study was called Listening to Women (LTW), because that is what women wanted it to be called, and that is the title used for publication, but it will eventually be changed to Listening to Pregnant and Postpartum People. When a woman comes in for prenatal care, she is told that her anxiety will be monitored throughout her pregnancy and postpartum period, just like her blood pressure and weight. This monitoring is done by text message on phones, and patients can fill out the screening information on their own time. A remote care coordinator reviews the data. If a woman screens positive for anxiety, the coordinator provides a brief intervention by devising a plan for addressing the woman's social and mental health needs and uses motivational interviewing to help her get to treatment where necessary. This information is

sent to the woman's primary care team. Screening occurs at the first prenatal care appointment, each trimester, 1 month after delivery, and every 3 months from delivery to 18 months postpartum.

The investigators piloted the LTW system in a large obstetrics practice, comparing women enrolled in LTW with the standard of care (i.e., in-person SBIRT from EHR data). The team found that women enrolled in LTW were 1.5 times more likely to be referred to treatment and 5 times more likely to actually go to treatment. Black women were less likely than White women to screen positive for anxiety with LTW screening than with in-person screening. However, Black women were significantly less likely to make it to treatment with in-person screening, which was not the case with LTW screening.

To get feedback on the LTW program and recommendations for modifications, the investigators conducted interviews with key informants via Zoom, with predominantly peripartum non-Hispanic Black people (96.5%) with and without mental health issues or SUDs. Sixty-nine women completed the interview. The mean age was 28, slightly more than 40% had a mood or anxiety disorder, about a third had an SUD that was primarily marijuana or alcohol, and about 25% had no mental health conditions. Respondents said that LTW was easy to use and not time-consuming. They were comfortable with the text method, especially when assured of confidentiality, and liked being able to express themselves in private without being seen or judged in person. They appreciated the convenience of being contacted by a care coordinator to help them navigate complex mental healthcare services. Dr. Guille said the respondents also provided insight into potential barriers to their discussing their mental health and SUDs, recalling Black cultural beliefs they heard growing up, including that mental health is a "White person problem" and "you don't go around talking about family business." There was also an element of distrust, both of the Department of Social Services intervening to take their children if mental health issues or SUDs were discovered and from the fact that the healthcare system usually let them down when they did try to talk about their problems, either by constantly changing their provider or by not accepting Medicaid and some insurances. Respondents also noted some helpful things that facilitated discussion of mental health and SUDs, such as having a Black healthcare worker and being reassured that postpartum depression is common and not something to be ashamed of.

Dr. Guille said modifications to LTW will include emphasizing to enrollees how private the system is, instituting more patient-provider concurrence in terms of race, addressing the areas of stigma and distrust that are barriers, and providing opportunities to see Black women speaking up about their mental health issues, to assure participants that they are not alone and not to blame. This might be done through a short video, because seeing others talk reassuringly about these issues makes people more willing to discuss their own challenges.

### *Discussion*

*Might the fact that the care coordinators help participants not only with mental health and SUD issues but also with social service needs account for some of the positive results of LTW?* **Dr. Guille** agreed, noting that people cannot prioritize their own health until basic needs like food and housing are taken care of. It would be interesting to see whether making women and their families feel stable and safe has any mediating effects.

*Is the in-person screening for depression a self-report of mood and anxiety disorders or a screening tool?* **Dr. Guille** said it is a universal standardized, structured screening tool that the providers use for in-person screening. The patients answer the specific questions.

*It is impressive to integrate the patient navigation and help with SDOH with this screening. It is a great role to add for lay healthcare workers and patient managers to do text-based screening and linkage to care. Which standardized screening tools are being used?* **Dr. Guille** said that in South Carolina, there is a universal screening tool that most providers use. If a woman positively answers any of the key substance use questions, she will be asked to complete a specific screening tool for substance use. If she positively answers certain questions about anxiety, she will complete the Edinburgh Postnatal Depression Scale.

### **Presentation: Postpartum Opioid-Related Mortality in Medicaid Patients**

*Elizabeth Suarez, Ph.D., Harvard Medical School*

Opioid overdose accounts for up to 10% of pregnancy-associated deaths. Women with opioid use disorders (OUDs) may also be particularly vulnerable to other causes of death in the postpartum period. These deaths have not been well characterized with population-based data. Medicaid covers approximately 75% of births for women with OUDs in the United States and provides an ideal vehicle for studying this population.

Dr. Suarez said that Aim 1 of her study was to describe the timing and risk factors for postpartum maternal deaths (between delivery and 1 year postpartum) attributable to opioid overdose and that Aim 2 was to describe the timing and causes of non-opioid overdose-related postpartum maternal deaths in women with OUDs. Data were obtained from the Medicaid Analytic eXtract (MAX) from 2006 to 2013 and the National Death Index (NDI) from 2007 to 2013. The linked MAX-NDI data showed 1,393 pregnancies (102 women with OUDs) with death between delivery and 1 year postpartum and 4,970,668 pregnancies (48,800 women with OUDs) without death.

For Aim 1, investigators used the Substance Abuse and Mental Health Services Administration (SAMHSA) ICD-10 definition of opioid-related overdose death. This definition requires a primary cause of death to be an overdose and a contributing cause of death to be specifically related to opioids. For Aim 2, causes of non-opioid-related deaths were categorized with SAMHSA ICD-10 primary cause codes (i.e., pregnancy, circulatory, cancer, suicide, homicide, accidental overdose, accidents, other diseases, and unknown cause). The researchers were able to define a series of risk factors for all the patients in the 3 months leading up to delivery, as well as the risk factors from delivery until the death date.

Dr. Suarez summarized the cumulative postpartum mortality results:

- The incidence of death in the year following delivery is six times higher in women with OUDs than among pregnant women in the general population, regardless of cause of death.
- For cumulative incidence of mortality by cause, the incidence of death by opioid overdose among pregnant women with OUDs was far greater than for any of the other SAMHSA causes of death except cancer for all pregnant women. The next most common

causes of death for pregnant women with OUDs were other overdoses, accidents, and suicides. In general, the incidence of death across all of the SAMHSA causes of death was much higher in the OUD population compared with pregnant women in the general population.

Dr. Suarez described the risk factors for opioid overdose death among all pregnant women, noting that White pregnant women had the highest risk. Other risk factors included maternal morbidity (e.g., obstetrics, mental health), SUDs other than opioids, opioid dispensing during pregnancy and in the postpartum period, numerous emergency department visits, and high postpartum healthcare utilization. Risk factors for opioid overdose death among pregnant women with OUDs were similar to the risk factors among all pregnant women with the exception of maternal morbidity. There was a strong predictive negative association of the use of opioid agonist therapy (OAT) in pregnancy and postpartum, with fewer deaths among those receiving treatment with buprenorphine and methadone.

Dr. Suarez summarized the findings of the study:

- Incidence of death, regardless of cause, in the year following delivery was six times higher in women with OUDs than in women in the general population.
- OAT was strongly associated with a reduced risk of opioid overdose death.
- Women with opioid overdose deaths had frequent contact with the healthcare system between delivery and death, potentially offering avenues of intervention.

### *Discussion*

*Is it possible to determine whether the women who are dying in the postpartum period from opioid overdoses are using drugs during pregnancy, or have they had period of abstinence and then restarted?* **Dr. Suarez** said active use cannot be captured from Medicaid data, although it was possible to see whether women were getting prescriptions for opioids, which was associated with opioid death.

*Why was fentanyl not included in the list of drugs causing death?* **Dr. Suarez** said the list was limited by the specific ICD-10 codes.

## **CONCLUSION AND THANKS**

*Courtney F. Aklin, Ph.D., Acting Associate Deputy Director, NIH, and NIH Maternal Mortality Task Force Co-Chair*

Dr. Aklin said this workshop should serve as an urgent reminder of the importance of IMPROVE and how much work remains to be done. There are too many instances of women being failed by the healthcare system, and there is a critical need to broaden the evidence base for new interventions and strengthen the understanding of the causes behind the disparities that were so eloquently discussed at this meeting. Dr. Clayton and Dr. Bianchi made it clear how important it is to move forward in this space.

Healthcare providers will benefit from a better understanding of how to look for signs of distress in their patients. Investigators will benefit from new collaborations, perhaps some coming from this meeting. And everyone must look for new targets for research, including the

role of healthcare coverage at the local and national levels and the promise of new digital technologies. The pandemic has added even more urgency into research on at disparities in care and the need to understand the effects of COVID-19, including long-term effects on pregnancy, as well as the physical, emotional, and socioeconomic impacts on all people.

Dr. Akin shared some thoughts about the 2021–2025 NIH strategic plan. The aspirational goal is to significantly reduce maternal deaths, particularly among Black and Alaska Native women. The Maternal Mortality Task Force will continue to play a leadership role in encouraging research on maternal health and maternal health disparities.

Dr. Akin thanked the presenters, the task force members, the attendees, and everyone who put together this incredible workshop for providing a platform for a continued conversation.

Dr. Bianchi thanked the moderators and contractors for a wonderful job and said she was encouraged that there will be new insights to put together pieces of this complex puzzle.

Dr. Clayton gave special thanks to the awardees, saying that the presentations at this meeting exemplified the importance of coming together and making the kinds of connections that will build and grow this field into the future.